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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/525,006

03/28/2005

Shirou Sawa

2005_0232A

1756

513 7590 06/03/2009

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EXAMINER

JAGOE, DONNA A

ART UNIT

PAPER NUMBER

1614

MAIL DATE

DELIVERY MODE

06/03/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/525,006	Applicant(s) SAWA ET AL.	
	Examiner Donna Jagoe	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 January 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 19-29,31-34,36-51,53-56 and 58-63 is/are pending in the application.
- 4a) Of the above claim(s) 39,40,61 and 62 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 19-29,31-34,36-38,41-51,53-56,58-60 and 63 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>3/11/09</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 19-29, 31-34, 36-51, 53-56 and 58-63 are pending in this application.

Claims 39, 40, 61 and 62 are withdrawn from further consideration.

Claims 19-29, 31-34, 36-38, 41-51, 53-56, 58-60 and 63 are rejected.

Applicants' arguments filed January 15, 2009 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Change of Examiner

The examiner assigned to the instant application has changed. The new examiner is Donna Jagoe. Contact information is provided at the end of this Office Action.

Priority

As recited in the Office Action dated September 27, 2007, Applicant is reminded that a certified translation has not been proved for the claim to foreign priority of JP2003-012427, filed 1/21/2003. Since no translation has been provided, prior art

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dates have been determined with reference to the priority date for the PCT application date, PCT/JP04/00350, filed 1/16/2004.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19-29, 31-34, 36-38, 41-51, 53-56, 58-60 and 63, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 19 and 41 recite an aqueous liquid preparation comprising at least 2-amino-3-(4-bromobenzoyl)phenylacetic acid (bromfenac) and an alkyl aryl polyether alcohol type polymer or polyethylene glycol fatty acid ester "wherein said liquid preparation is in the form of an eye drop". It is unclear what is meant by "in the form of an eye drop. Is this aqueous liquid preparation in a container shaped like an eye drop? It is suggested that the claim be amended to recite "wherein said liquid preparation is formulated for ophthalmic administration".

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 19-29, 31-34, 36-38, 41-51, 53-56, 58-60 and 63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hellberg et al. (US 5,998,465; 1999) and

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Nolan, et al. ("The topical anti-inflammatory and analgesic properties of bromfenac in rodents; Agents and Actions; 1988 Aug; 25(1-2):77-85; cited with previous Interview Summary).

Hellberg teaches pharmaceutical compositions of anti-inflammatory compounds (abstract); the compounds include a non-steroidal anti-inflammatory moiety (NSAIA) and an antioxidant moiety linked through an ester bond formed by the carboxylic acid moiety of the NSAIA (col. 2, lines 20-24); NSAIA moieties include bromfenac (col. 3, line 57; claim 5); examples 2 and 3 (col. 11) teach topical ophthalmic formulations useful for treating inflammation, both of these formulations include tyloxapol at 0.01-0.05 w/v %, HPMC (thickener), benzalkonium chloride (preservative), edetate disodium (chelating agent) (col. 11, Examples 2-3); the pH is adjusted to 7.4 (about 7.5; col. 11, line 64); topical formulations administered by drops (eye drops; col. 10, lines 15-18). Hellberg does not teach bromfenac (only the ester of bromfenac). Nolan teaches bromfenac (the sodium salt, sesquihydrate form) was effective as a topical analgesic at concentrations of 0.1-0.32 % in mice and more potent than the other drugs tested (abstract). It would have been obvious for one of ordinary skill in the art at the time of the invention to substitute bromfenac, taught by Nolan for the compounds of Hellberg in the example formulation giving formulations of the instant claims and to select concentrations of bromfenac sodium, sesquihydrate of 0.1, about 0.2 and about 0.32 %, in the invention of Gamache, since these values have demonstrated efficacy for topical use. It would also have been obvious to adjust the concentration of tyloxapol, to optimize the formulations for the effect would on the solubility and stability of the aqueous

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preparations, which would have resulted in the effective tyloxapol concentrations of about 0.02 and 0.3 w/v%, recited in claims 25 and 32. The motivation to substitute bromfenac in the Hellberg formulations would have been the art-recognized equivalent activity of bromfenac as an anti-inflammatory agent in topical usage. The motivation to adjust concentrations would have been the routine optimization of these topical ophthalmic formulations for anti-inflammatory use in the eye.

Claims 19-29, 31-34 and 36-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gamache, et al. (WO 01/15677 A2; 03/2001; previously cited) and ISTA Pharmaceuticals ("New Drug Applications: Xibrom", http://www.drugs.com/nda/xibrom_040525.html, accessed online 9/19/2007; previously cited) or Nolan, et al. ("The topical anti-inflammatory and analgesic properties of bromfenac in rodents; Agents and Actions; 1988 Aug; 25(1-2):77-85; provided with Interview Summary).

Gamache teaches compositions for otic and intranasal use (p.6, lines 5-6) that contain a combination of a 5-HT agonist and an anti-inflammatory agent (p. 6, lines 1-4; p. 12 lines 9-10) or alternatively sequential or concurrent dosing of separate compositions that contain the 5-HT antagonist in one composition and the anti-inflammatory agent in a second composition (p. 12, lines 9-11); specifically claimed is the anti-inflammatory species bromfenac (2-amino-3-(4-bromobenzoyl)phenylacetic acid). Typical concentrations of anti-inflammatory agents, such as bromfenac, are taught in the range 0.01-1.0 % (w/v) (overlapping with 0.01-0.5; p. 13, lines 6-8);

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aqueous formulations are preferred (p. 10, lines 11-14); tyloxapol is taught in a concentration of 0.05 % (w/v) (p. 16, line 30). It is noted that instant claim 21 and further dependent claims limit the options for the salt of bromfenac to the sodium salt, and that the specific concentrations recited in dependent claims apply to the sodium salt; the other options (bromfenac or a hydrate of bromfenac) are still viable choices that are part of instant claim 21 claims depending therefrom (which depend on and include the options of claim 20). Gamache teaches bromfenac in the concentration range of claim 20 (which is also an option of claims 21-24 and 31). The salt form of bromfenac in solution will be the same when the acid is dissolved in a solution followed by adjustment to the desired pH with NaOH/HCl (Gamache, p. 15, line 33) as when the sodium salt is dissolved in solution adjusted to the same pH; in this case Gamache also teaches the sodium salt limitation of instant claim 21, albeit not the sodium salt concentration limitation of instant claim 22 and further dependent claims, since the claim is drawn to an aqueous liquid preparation, irrespective of how it is prepared. However, the concentration range of 0.01-1.0% overlaps and encompasses the claimed concentration range of the sodium salt of bromfenac instantly claimed.

The ISTA Pharmaceuticals news release demonstrates that products containing 0.1 % bromfenac sodium acquired US marketing rights for Xibrom in May 2002 (were known by others in this country before applicant's priority date, a 35 USC 102(a) date). Nolan teaches bromfenac (the sodium salt, sesquihydrate form) was effective as a topical analgesic at concentrations of 0.1-0.32 % in mice and more potent than the other drugs tested (abstract). It would have been obvious for one of ordinary skill in the art at

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the time of the invention to select concentrations of bromfenac sodium, sesquihydrate of 0.1, about 0.2 and about 0.32 %, in the invention of Gamache, since these values have demonstrated efficacy for topical use. It would have been obvious to adjust the concentration of tyloxapol, to see what the effect would be on the solubility and stability of the aqueous preparations, which would have resulted in the effective concentrations of the instant claims. It would also have been obvious to adjust the pH to values in the 7.5 to 8.5 range, with the potential of dissolving and/or stabilizing more of the acidic drug, bromfenac, in a more aqueous soluble ionic form. The motivation would have been to prepare pharmaceutical products with optimal drug dosage and stability.

Double Patenting

Claims 19-29, 31-34, 36-38, 41-51, 53-56, 58-60 and 63 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-43 of copending Application No. 11/755662.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application contains claims drawn to method of treating pain and/or inflammation associated with an ocular condition, by administering the aqueous solutions of the instant claims. It would have been obvious to one of ordinary skill in the art at the time of the invention to use the formulations of the instant claims in the methods of the copending application, since the claims recite that the

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formulations are eye drops, and the instant abstract also teaches some of the conditions treated of the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicant asserts that Gamache et al. in view of ISTA or Nolan et al. does not teach the claimed invention because the amended claims require that the aqueous liquid preparation is in the form of an eye drop. In response, please see the rejection supra regarding claims drawn to the composition "in the form of an eye drop". Further, Gamache teaches the composition to be employed intranasally and intraotically. There is nothing differentiating the composition of the instant claims from the composition of Gamache other than the claim that it is "in the form of an eye drop". Drops that are formulated for intranasal use and otic use are sterile and isotonic. The intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. Since the drops of Gamache are capable of performing the intended use, then it meets the claim.

Regarding the inclusion of other agents in the drops of Gamache, The claim language *comprising* leaves the claim open for the inclusion of unspecified ingredients, even in major amounts. Applicant asserts that the tyloxapol is only mentioned as being added to an 1B/1D agonist and moxifloxacin in example 4 with no explanation of why it is

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included. In response, a reference is not limited to working examples. *In re Fracalossi* 215 USPQ 569 (CCPA 1982). Applicant asserts that Gamache et al. is silent regarding the alkyl aryl polyether alcohol type polymer or a polyethylene glycol fatty acid ester component according to the claimed eye drop. In response, Gamache et al. teach polysorbate 20, 60, and 80 as a surfactant or co-solvent (see page 12).

Applicant asserts that the intended purpose of the invention disclosed in Hellberg et al. is to provide compounds having anti-inflammatory activity and antioxidant activity and further asserts it would not be obvious to substitute bromfenac. In response, bromfenac is clearly disclosed as a compound that is contemplated for use in the invention of Hellberg et al. (see claims 5 and 19 of the patent). "Products of identical chemical composition (i.e. bromfenac) can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims (i.e. anti inflammatory and antioxidant activity) are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990) (Applicant argued that the claimed composition was a pressure sensitive adhesive containing a tacky polymer while the product of the reference was hard and abrasion resistant. "The Board correctly found that the virtual identity of monomers and procedures sufficed to support a prima facie case of unpatentability of Spada's polymer latexes for lack of novelty.").

In response to applicant's argument that Hellberg et al. is nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the

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applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, Hellberg et al. teach a composition for intraocular administration comprising inter alia, a compound (bromfenac) and tyloxapol (see examples).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-

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0576. The examiner can normally be reached on Monday through Friday from 8:00 A.M. - 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Donna Jagoe /D. J./
Examiner
Art Unit 1614

May 30, 2009

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614